REMARKS

Claims 1, 2, 4-14, 16-18, 22-24 and 26-57 are pending. Claims 3, 15, 19-21 and 25 have been canceled without prejudice. It is respectfully submitted that no new matter has been added by virtue of this amendment.

I. RENUMBERING OF CLAIMS

In the Office Action, the Examiner indicated that claims 38-57 were renumbered according to rule 126 since there were no claims 36 and 37 following claim 35. In response, the Examiner is directed to page 29 of the specification as filed which recites claims 36 and 37. Accordingly, the Examiner is requested to further examine the claims in view of the original numbering.

II. REJECTION UNDER 35 U.S.C. § 112

In the Office Action, claims 1-53 were rejected under 35 U.S.C. § 112, first paragraph on the grounds that "the specification... does not reasonably provide enablement for generic agent combined with a particulate carrier or various particles claimed in claim 2." The Examiner further stated that the "instant specification does not provide adequate support for the broadly claimed 'antiseptic', anti-inflammatory agents and wound healing promoting agents and 'particulate carrier'... the specification also does not adequately describe what 'functional and cosmetic tissue remodeling' is and how the method is practiced as claimed in the method claims...[i]nstant specification also does not teach how one can apply topically to the respiratory tract and treat or prevent diseases such as HIV and opportunistic diseases."

In response, the claims have been amended as not to recite a "generic agent". The claims, as amended, are now directed to antiseptic or wound healing agents. It is respectfully submitted that the pending claims do provide adequate support for these claim terms.

With respect to antiseptic agents, the Examiner is directed to page 5, lines 1-4, which states that "antiseptic agents are understood to include those disinfecting agents which are pharmaceutically acceptable and suitable for the lower respiratory tract..." Further, page 5, lines 6-11 provides specific examples of antiseptic agents which are known to one skilled in the art.

With respect to wound healing agents, the Examiner is directed to page 5, lines 13-15 which defines such agents as agents which promote granulation and epithelization. This is followed by specific examples of wound healing agents which are known to one skilled in the art.

With respect to particulate carrier, the Examiner is directed to page 3, lines 16-24 which provides particulate carriers known to one skilled in the art, such as liposomes, microspheres, nanoparticles, large porous particles and individually coated drug substance molecules. The Examiner is further directed to page 9 which sets forth various prior art documents which teach the preparation of such particulate carriers. It is noted that "the law does not require a specification to be a blueprint in order to satisfy the requirement for enablement under 35 U.S.C. 112, first paragraph," *Staehlin v. Secher, 24 U.S.P.Q. 2d. 1513, 1516 (Bd. Pat. App. & Int. 1992)* and that "a specification need not describe -- and best omits – that which is well known in the art. See, e.g., *In re Buchner, 929 F.2d 660, 661, 18 U.S.P.Q. 2d 1331, 1332 (Fed. Cir. 1991).*

With respect to "functional and cosmetic tissue remodeling" the Examiner is directed to page 5, lines 27 to page 6, line 7 which states the following:

> *...it is known that body tissue repair may be accompanied by the formation of scar tissue, which can be functionally and/or cosmetically harmful, or at least undesirable. Hyperkeratosis and the uncontrolled proliferation of tissue may cause serious harm, leading to dysfunctions, and may of course also be cosmetically undesirable. After infections and inflammations, re-growing or healing tissue may cause neoplasms and intergrowth...*

In view of this teaching in the specification, it is submitted that one skilled in the art would understand the meaning of the term "functional remodeling" as tissue repair and tissue growth produced in the location of a previous infection, lesion or open wound which results in, e.g., restored blood flow to an injured area; and the term "cosmetic remodeling" results when previously damaged tissue is repaired so that scarring or hyperkeratosis is reduced or prevented, resulting in minimal or no visible signs of previous damage. However, to advance the prosecution of the application, the term "cosmetic" has been removed from the pending claims

With respect to the Examiner's statement that the "specification also does not teach how one can apply topically to the respiratory tract and treat or prevent diseases such as HIV and opportunistic diseases", the Examiner is directed to page 6, lines 22-29, page 7, lines 1-14, page 11, lines 1-21, 26-29 and page 12, lines 1-4, wherein specific administration routes and dosage forms are described. These include respiratory tract administration via nebulization or dry powder inhalation via pneumatic pump applicators, two-chamber gas pressure packs and aerosol spray dispensers. Further, it is pointed out to the Examiner that the presently claimed invention and methods cannot be used to prevent diseases such as HIV, but rather to treat and alleviate such diseases, e.g., by treating opportunistic infections which are known to one skilled in the art to be associated with such diseases as discussed on page 11, lines 15-21 of the specification.

In view of the arguments presented, it is respectfully submitted that the present application enables one skilled in the art to practice the present invention as recited in the pending claims and the Examiner is requested to remove the § 112, first paragraph rejections.

III. REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH:

In the Office Action, the Examiner rejected claims 1-53 under 35 U.S.C. § 112, second paragraph, as being indefinite on several grounds.

With respect to the rejection on the grounds that "it is unclear what applicant intends to convey by healing wounds to the lower respiratory tract," the Examiner is directed to page 5, line 27 to page 6, line 7 of the specification which describes problems associated with tissue repair in order to prevent or reduce scarring and hyperkeratosis associated with wounds which can be present in the lower respiratory tract due to, e.g. lower respiratory infections.

With regard to the Examiner's statement that "the distinction between liposomes and microspheres and nanoparticles in claim 2 is unclear" it is respectfully submitted that these terms are known to one skilled in the art as separate and distinct carrier particles. Microspheres are known in the art from, e.g., WO 95/15118, as set forth in the specification on page 9, lines 1-5 and nanoparticles are known in the art as described by Heyder, as set forth on page 9, lines 6-10 of the specification.

With respect to the rejection of the term "large", it is respectfully submitted that this term in the context it is used, is not a relative term. Rather, the word large should be read as part of the art recognized term "large porous particle", which is known in the art from, e.g., Edward et al. as set forth on page 9, lines 18-22 of the specification.

With respect to the rejection of the term "laser pulse polymer coated molecule preparation", it is respectfully submitted that this term is known to one skilled in the art as a preparation prepared in accordance with art known laser pulse polymer coating technology as described by, e.g., Talton er al. as set forth on page 9, lines 12-16 of the specification.

With respect to the terms "greatest", "such as", "including", and "in case", the claims have been amended to delete these terms.

With respect to the rejection of claims 4, 5, 7, 19 and 27 based on improper Markush format, the claims have been amended to the proper format.

With respect to the statement that "the distinction between antiseptic and wound healing promoting agent in claims 8 and 22 is unclear" , the Examiner is directed to page 5, lines 1-15 which describes that "antiseptic agents" are agents which are disinfecting agents and "wound-healing agents" are agents which promote granulation and epithelization.

With respect to the Examiner's statement, "which carrier particles are being referred to in claims 9, 10, 32, 40 and 53" it is noted that these claims are dependent claims and any particles which are encompassed by a parent claim, but do not fall within the further limiting size range of a dependent claim, are not encompassed by the dependent claim.

With respect to the rejection of the terms "conserving agents" and "consistency forming agents", it is respectfully submitted that one skilled in the art would understand these terms as encompassing pharmaceutically acceptable excipients which provide the designated function.

With regard to the rejection of claim 15, this claims has been canceled

With respect to the rejections of claims 16 and 37, (i) a "compacted solid medicament reservoir" and a "ring tablet" are compacted dosage forms which are suitable for the generation of inhalable particles as known to one skilled in the art; (ii) the term "dispersion" has been deleted from the claims; and (iii) the claims now recite that the nebulized or aerosolized particulate carrier is derived from a solution.

With respect to the rejections of claim 17, one skilled in the art would readily understand that the lower respiratory tract includes the larynx, trachea, bronchi and alveoli. In contrast the upper respiratory tract comprises the ears, nose, mouth and throat. In addition, it is known in the art that the size of a particle determines where the particle is deposited within the respiratory tract during inhalation administration as set forth on page 8, lines 23-27. Further, in response to the Examiner's inquiry, particles which are administered to the lower respiratory tract must pass

through the upper respiratory tract.

With respect to the rejection of claims 21 and 23, "functional tissue remodeling" is described in the specification from page 5, lines 27 to page 6, line 7 as tissue repair and tissue growth produced in the location of a previous infection, lesion or open wound which results in, e.g., restored blood flow to an injured area. "Cosmetic remodeling" has been deleted from the present claims.

Claims 22 and 23 have been amended to recite "administration" to the lower respiratory tract. Such administration is readily known to one skilled in the art as the inhalation of inhalable particles, e.g., nebulized or aerosolized particles.

In view of the arguments presented, it is respectfully submitted that the present application enables one skilled in the art to practice the present invention as recited in the claims and the Examiner is requested to remove the § 112, second paragraph rejections.

IV. DOUBLE PATENTING REJECTIONS:

In the Office Action, claims 1-53 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-48 of copending Application No. 09/701,220 and claims 1-21 and 40-46 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 5,863,556.

In response, Applicants submit that upon indication that the claims are otherwise allowable, the filing of terminal disclaimers will be considered.

V. **REJECTIONS UNDER 35 U.S.C. § 102(b):**

In the Office Action, the Examiner rejected claims 1-3, 9, 11, 12, 14-16, 19-26, 32, 34-37, 43, 44, 46-47, 49, 50 and 52-53 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,049,388 ("the Knight patent"). The Examiner stated that "Knight discloses liposome aerosol formulation for the delivery of drugs to respiratory tract...". The particle sizes are 1-5 microns. The drugs include antibiotics, antiviral agents and steroids...."

Claims 1-3, 9, 11, 12, 14-16, 19-26, 32, 34-37, 43, 44, 46-47, 49, 50 and 52-53 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,049,389 ("the Radhakrishnan patent"). The Examiner stated that Radhakrishnan discloses liposome aerosol formulation for the delivery of drugs to respiratory tract. The particle sizes are 1-5 microns. The drugs include antibiotics, antiviral agents and steroids...."

Claims 1-3, 9, 11, 12, 14-16, 19-26, 32, 34-37, 43, 44, 46-47, 49, 50 and 52-53 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,290,540 ("the Prince patent"). The Examiner stated that Prince discloses liposome aerosol formulation for the delivery of drugs to respiratory tract. The particle sizes are 1-10 microns. The drug combination include antibiotics, antiviral agents and steroids...."

In response, the Examiner is directed to the independent claims of the present invention which are directed to inhalable compositions comprising antiseptic agents or agents which promote the healing of wounds and methods thereof. It is respectfully submitted that neither the Knight patent, the Radhakrishnan patent nor the Prince patent teach or suggest antiseptic agents or agents which promote the healing of wounds in the compositions and methods described therein. Accordingly, the claims are not anticipated by these references and the Examiner is requested to withdraw these rejections.

Claims 1-21 and 40-46 were rejected under 35 U.S.C. § 102(b) as being anticipated by JP-7-145081 or EP 0 639 373. The Examiner stated that the JP and EP references disclose the same composition as the present claims.

This rejection is respectfully traversed. The JP and EP references disclose liposomal preparations useful in the treatment of external wounds. These references do not teach or suggest the formulations disclosed therein as useful for treatment of the lower respiratory tract as encompassed by the independent method claims of the present invention. Further, these references do not teach or suggest the formulations disclosed therein in nebulized or aerosolized form as recited in the present composition claims. Rather, the formulations disclosed in the JP and EP references are in form suitable for topical administration, e.g. creams. Accordingly, the Examiner is requested to remove the anticipation rejections over these references.

V. REJECTION UNDER 35 U.S.C. § 103(a):

In the Office Action, the Examiner rejected claims 22-39 and 47-53 under 35 U.S.C. § 103(a) as being unpatentable over the Knight or the Radhakrishnan or the Prince patents. The Examiner stated that "Knight, Radhakrishnan and Prince do not teach the administration of the composition for the infections which occur during cosmetic surgery. However, it is deemed obvious to one of ordinary skill in the art that the wound healing compositions can be applied during any state wherein the wounds are susceptible to infectious agents, with the expectation of similar anti-septic effect."

This rejection is respectfully traversed, at the very least, as the claims are now directed to antiseptic agents and wound healing agents as disclosed in the specification. As the Knight, Radhakrishnan and Prince references do not teach or suggest the presently claimed compositions as presented above with respect to the anticipation rejections, it would not be obvious in view of these references to utilize such compositions in the presently claimed methods.

In the Office Action, the Examiner rejected claims 22-39 and 47-53 under 35 U.S.C. § 103(a) as being unpatentable over JP or EP in combination with Knight or Radhakrishnan or Prince.

These rejections are respectfully traversed, at the very least, as the JP and EP references are not properly combinable with either the Knight, Radhakrishnan and Prince references. The JP and EP references are directed to external treatments, while the secondary references are directed to pulmonary treatment. Accordingly, one skilled in the art would not be motivated to combine these references. Accordingly, the Examiner is requested to remove the rejection under 35 U.S.C. § 103(a).

CONCLUSION:

Applicants respectfully submit that in view of the amendments made and arguments presented, the present application is in condition for allowance.

A check in the amount of $1160.00 is enclosed, $980.00 of which is for the petition for three-month extension of time. If it is determined that additional fees are due or that any fee has been overpaid, the Commissioner for Patents is hereby authorized to charge said fee or credit any overpayment to Deposit Account No. 50-0552.

Respectfully submitted,

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Marked-Up Amended Claim Version

1. (Twice Amended) A pharmaceutical preparation for the application of antiseptic agents or agents which promote the healing of wounds to the lower respiratory tract, [wherein the preparation contains at least one of said agents] comprising aerosolized or nebulized inhalable particulate carriers suitable for administration into the lower respiratory tract combined with an agent selected from the group consisting of an antiseptic agent, a wound-healing agent or a combination thereof [combined with a particluate carrier].

4. (Twice Amended) The preparation of claim 1, wherein the antiseptic agent is selected from the group consisting of oxygen- releasing compounds, [and] halogen-releasing compounds, metal compounds, [such as silver compounds, mercury compounds;] organic disinfectants, [including inter alia formaldehyde-releasing compounds,] alcohols, phenols, [including alkylphenols arylphenols as well as halogenated phenols] quinolines [and], acridines, hexahydropyrimidines, quaternary ammonium compounds [and], iminium salts,[and] guanidines and combinations thereof.

5. (Twice Amended) The preparation according to claim 4, wherein the antiseptic agent is selected from the group consisting of [comprising] metal compounds, [such as mercury compounds,] phenol, phenol derivatives, [such as thymol, eugenol, hexachlorophene] iodine, [and] iodine complexes and combinations thereof.

7. (Twice Amended) The preparation according to claim 1, wherein the wound-healing promoting agent is selected from the group consisting of [agents promoting granulation and epithelization such as] dexpanthenol, allantoines, azulenes, tannines, [compounds from the] vitamin B [series, or similarly acting agents] compounds and combinations thereof.

9. (Twice Amended) The preparation of claim 1, wherein the carrier particles[,] have a [substantially uniform] size in the range of between 1 and about 50 μm.

10. (Twice Amended) The preparation of claim 9, wherein the carrier particles[,] have a [substantially uniform] size in the range of between 20 and about 30 μm diameter for application to the traches.

16. (Twice Amended) The preparation of claim 1, wherein, the aerosolized or nebulized carrier particles are derived from [preparation comprises] a compacted solid medicament reservoir, a ring-tablet, a gelatin capsule, a powder, a spray, an emulsion, a dispersion, a suspension or a solution containing the carrier and agent or agents in a pharmaceutically acceptable solid or liquid formulation, which is suitable for the generation of inhalable particles.

17. (Twice Amended) The preparation of claim 1, [comprising a suitable form for administration via the lower respiratory tract, which comprises] wherein said particulate carrier comprises:

(a) liposomes comprising a pharmaceutically acceptable liposome membrane forming substance; and

(b) a 0.1 to 2% PVP iodine solution [(at approximately 10% available iodine in the PVP iodine complex [) at least most of which is encapsulated by said liposome membranes], wherein the liposomes are in a [of substantially uniform] size between about 1μm and about 50μm[, and the formulation additionally comprises customary additives, adjuvants and auxiliary substances of a pharmaceutical solution or dispersion formulation].

18. (Twice amended) The preparation according to claim 17, [characterised in that] wherein the liposomes are [of a substantially uniform] in a size [, in the] range between 20μm and 30μm diameter for application to the trachea.

22. (Twice Amended) A method of [preventing or] treating infections of the lower respiratory tract in a human or animal [lower respiratory tract] comprising[; applying, to said tract] administering a pharmaceutical preparation to the lower respiratory tract, said preparation comprising an inhalable particulate carrier combined with an agent selected from the group consisting of an antiseptic agent, a wound-healing agent or a combination thereof [at least one of an antiseptic agent or a wound-healing promoting agent combined with a particulate carrier in said preparation].

23. (Twice Amended) A method of providing functional [and cosmetic] tissue remodeling and repair in the lower respiratory tract in a human or animal [lower respiratory tract] comprising [; applying, to said tract] administering a pharmaceutical preparation to the lower respiratory tract comprising an inhalable particulate carrier combined with an agent selected from the group consisting of an antiseptic agent, a wound-healing agent or a combination thereof [comprising at least one of an antiseptic agent or a wound-healing promoting agent].

24. (Twice Amended) The method of claim 22 or 23, wherein said particulate carrier [comprises at least one] is selected from the group consisting of a liposome preparation, a microsphere preparation, a nanoparticle preparation, a Large Porous Particle preparation [or] a laser-pulse polymer coated molecule preparation and a combination thereof.

27. (Twice Amended) The method of claim 22 or 23, wherein the antiseptic agent is selected from the group consisting of oxygen- releasing compounds, [and] halogen-releasing compounds, [;] metal compounds, [such as silver compounds, mercury compounds;] organic disinfectants, [including inter alia formaldehyde-releasing compounds,] alcohols, phenols [including alkylphenols arylphenols as well as halogenated phenols], quinolines [and], acridines, hexahydropyrimidines, quaternary ammonium compounds [and], iminium salts, [and] guanidines and a combination thereof.

28. (Twice Amended) The method of claim 22 or 23, wherein the antiseptic agent is selected from the group consisting of [comprising] metal compounds, [such as mercury compounds,] phenols, phenol derivatives[, such as thymol, eugenol, hexachlorophene] iodine, [and] iodine complexes and a combination thereof.

30. (Twice Amended) The method of claim 22 or 23, wherein the wound-healing promoting agent is selected from the group consisting of [agents promoting granulation and epithelization such as] dexpanthenol, allantoines, azulenes, tannines, [compounds from the] vitamin B [series, or similarly acting agents] compounds and a combination thereof.

32. (Twice Amended) The method of claim 22 or 23, wherein the carrier particles[, especially liposomes] have a [substantially uniform] size in the range between about 1 μm and about 50 μm.

33. (Twice Amended) The method according to claim 32, wherein the carrier particles have a [substantially uniform] size in the range between 20 μm and 30 μm diameter for application to the trachea.

38. (Twice Amended) The method of claim 22 or 23, wherein the particulate carrier is [preparation comprises a] suitable [form] for administration via [the lower respiratory tract comprising an active-agent loaded carrier, wherein the carrier is in the form of liposomes, in the form of an aerosol, or in the form of powder aerosol] nebulization or aerolsolization.

40. (Amended) The method of claim 22 or 23, [the preparation being in a suitable form for administration via the lower respiratory tract, which] wherein said particulate carrier comprises:

(a) liposomes comprising a pharmaceutically acceptable liposome membrane forming substance; and

(b) a 0.1 to 2% PVP iodine solution [(at approximately 10% available iodine in the PVP iodine complex) at least most of which is encapsulated by said liposome membranes], wherein the liposomes are in a [of substantially uniform] size between about 1μm and about 50μm[, and the formulation additionally comprises customary additives, adjuvants and auxiliary substances of a pharmaceutical solution or dispersion formulation].

41. (Twice Amended) The method of claim 22 or 23, wherein the liposomes are[of a substantially uniform] in a size [in the] range between 20 μm and 30 μm diameter for application to the trachea.

44. (Amended) The preparation according to claim 9, wherein the carrier particles [,] have a [substantially uniform] size in the range between 1μm to about 30μm.

45. (Amended) The preparation according to claim 10, wherein[,] the carrier particles [,] have a [substantially uniform] size in the range between about 10μm and 20μm diameter for application to the bronchi.

46. (Amended) The preparation according to claim 10, wherein[,] the carrier particles [,] have a [substantially uniform] size in the range between 1μm and 6μm diameter for application to the alveoli.

47. (Amended) The preparation according to claim 10, wherein[,] the carrier particles [,] have a [substantially uniform] size in the range between 2μm and 5μm diameter for application to the alveoli.

48. (Amended) The preparation according to claim 17, wherein the liposomes [are of a substantially uniform] have a size[,] in the range of 10μm and 20μm diameter for application to the bronchi.

49. (Amended) The preparation according to claim 17, wherein the liposomes [are of a substantially uniform] have a size[,] in the range of 1μm and 6μm diameter for application to the alveoli.

50. (Amended) The preparation according to claim 17, wherein the liposomes [are of a substantially uniform] have a size[,] in the range of 2μm and 5μm diameter for application to the alveoli.

51. (Amended) The method of claim 22 or 23, wherein the carrier particles have a [substantially uniform] size in the range between about 1μm and about 30μm.

52. (Amended) The method according to claim 32,wherein the carrier particles have a [substantially uniform] size in the range between 10μm and 20μm diameter for application to the bronchi.

53. (Amended) The method according to claim 32, wherein the carrier particles have a [substantially uniform] size in the range between 1μm and 6μm diameter for application to the alveoli.

54. (Amended) The method according to claim 32, wherein the carrier particles have a [substantially uniform] size in the range between 2μm and 5μm diameter for application to the alveoli.

55. (Amended) The method of claim 22 or 23, wherein the liposomes have a [are of a substantially uniform] size in the range between 10μm and 20μm diameter for application to the bronchi.

56. (Amended) The method of claim 55, wherein the liposomes have a [are of a substantially uniform] size in the range between 1μm and 6μm diameter for application to the alveoli.

57. (Amended) The method of claim 56, wherein the liposomes have a [are of a substantially uniform] size in the range between 2μm and 5μm diameter for application to the alveoli.